

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
20 December 2001 (20.12.2001)

PCT

(10) International Publication Number  
WO 01/96295 A3

(51) International Patent Classification<sup>7</sup>: C07D 401/12.  
207/16, 403/12, 417/12, 409/12, A61K 31/40, 31/4439,  
31/506, 31/428, 31/427, A61P 3/10

(74) Agent: BECKER, Konrad; Novartis AG, Corporate In-  
tellectual Property, Patent & Trademark Dept., CH-4002  
Basel (CH).

(21) International Application Number: PCT/EP01/06595

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,  
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,  
MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,  
SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,  
ZW.

(22) International Filing Date: 11 June 2001 (11.06.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
09/592,336 13 June 2000 (13.06.2000) US

(84) Designated States (*regional*): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian  
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European  
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,  
IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF,  
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except AT, US*): NO-  
VARTIS AG [CH/CH]; Lichtstrasse 35, CH-4056 Basel  
(CH).

**Published:**

— with international search report

(71) Applicant (*for AT only*): NOVARTIS-ERFINDUNGEN  
VERWALTUNGSGESELLSCHAFT M.B.H [AT/AT];  
Brunner Strasse 59, A-1230 Vienna (AT).

(88) Date of publication of the international search report:  
16 May 2002

(72) Inventor; and

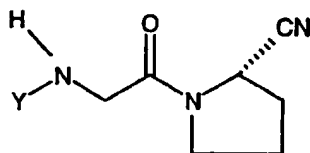
(75) Inventor/Applicant (*for US only*): VILLHAUER, Ed-  
win, Bernard [US/US]; 20 Dorothy Drive, Morristown, NJ  
07960 (US).

*For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.*



WO 01/96295 A3

(54) Title: 2-CYANOPYRROLIDINE DERIVATIVES AND THEIR USE AS MEDICAMENTS



(I)

(57) Abstract: The present invention relates to certain N-(substituted glycy)-2-cyanopyrrolidines of formula (I) wherein Y is as defined herein, in free form or in acid addition salt form. Compounds of formula (I) inhibit DPP-IV (dipeptidyl-peptidase-IV) activity. They are therefore indicated for use as pharmaceuticals in inhibiting DPP-IV and in the treatment of conditions mediated by DPP-IV, such as non-insulin-dependent diabetes mellitus, arthritis, obesity, osteoporosis and further conditions of impaired glucose tolerance.

# INTERNATIONAL SEARCH REPORT

national Application No  
PCT/EP 01/06595

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D401/12 C07D207/16 C07D403/12 C07D417/12 C07D409/12  
A61K31/40 A61K31/4439 A61K31/506 A61K31/428 A61K31/427  
A61P3/10

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98 19998 A (CIBA GEIGY AG; VILLHAUER EDWIN BERNARD (US)) 14 May 1998 (1998-05-14) claims; examples 1-66 ---	1-10
Y	US 6 011 155 A (VILLHAUER EDWIN BERNARD) 4 January 2000 (2000-01-04) claims; examples ---	1-10
Y	T. E. HUGHES ET AL.: "(1-''2-(5-Cyanopyridin-2-yl!amino!-acetyl!-2-cyano(S)-pyrrolidine), a Slow-Binding Inhibitor of Dipeptidyl Peptidase IV" BIOCHEMISTRY, vol. 38, no. 36, 1999, pages 11597-11603, XP002184055 page 11597, abstract; page 11598, Chart 1 --- -/--	1-10

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*G\* document member of the same patent family

Date of the actual completion of the international search

26 November 2001

Date of mailing of the international search report

10/12/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.  
Fax: (+31-70) 340-3016

Authorized officer

Hass, C

## INTERNATIONAL SEARCH REPORT

national Application No

PCT/EP 01/06595

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	BALKAN B ET AL: "INHIBITION OF DIPEPTIDYL PEPTIDASE IV WITH NVP-DPP728 INCREASES PLASMA GLP-1 (7-36 AMIDE) CONCENTRATIONS AND IMPROVES ORAL GLUCOSE TOLERANCE IN OBESE ZUCKER RATS" DIABETOLOGIA, BERLIN, DE, vol. 42, no. 11, November 1999 (1999-11), pages 1324-1331, XP000921066 ISSN: 0012-186X page 1324, abstract; page 1325, figure 1 ----	1-10
A	EP 0 419 683 A (JAPAN TOBACCO INC; YOSHITOMI PHARMACEUTICAL (JP)) 3 April 1991 (1991-04-03) page 30, line 1 - line 12; claims -----	1-10

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-3, 7-10 (all partly)

Compounds of formula (I) wherein Y is a substituted 1,1-dimethylethyl group, and their pharmaceutical use

2. Claims: 1-3, 7-10 (all partly), 4-6

Compounds of formula (I) wherein Y is a substituted cyclohexyl group, and their pharmaceutical use

3. Claims: 1-3, 7-10 (all partly)

Compounds of formula (I) wherein Y is a substituted piperidiny group, and their pharmaceutical use

4. Claims: 1-3, 7-10 (all partly)

Compounds of formula (I) wherein Y is a carbobicyclic system, and their pharmaceutical use

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 01/06595

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9819998	A	14-05-1998	AU 726186 B2	02-11-2000
			AU 5318498 A	29-05-1998
			BR 9714130 A	29-02-2000
			CN 1236361 A	24-11-1999
			CZ 9901615 A3	11-08-1999
			WO 9819998 A2	14-05-1998
			EP 0937040 A2	25-08-1999
			HU 0000323 A2	28-08-2000
			JP 3217380 B2	09-10-2001
			JP 2000511559 T	05-09-2000
			NO 992028 A	28-04-1999
			PL 332777 A1	11-10-1999
			SK 60899 A3	10-04-2000
			TR 9901004 T2	21-07-1999
US 6011155	A	04-01-2000	US 6124305 A	26-09-2000
EP 0419683	A	03-04-1991	EP 0419683 A1	03-04-1991
			WO 9012005 A1	18-10-1990
			US 5118811 A	02-06-1992

**THIS PAGE BLANK (USPTO)**